

Avosentan reduces proteinuria but causes serious side effects

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The drug avosentan substantially reduces urinary protein loss in people with type 2 diabetes and kidney disease, but the drug causes serious side effects, according to a study appearing in an upcoming issue of the *Journal of the American Society Nephrology* (JASN). The results suggest that lower doses of avosentan may have a more favorable risk/benefit ratio for patients.

Despite aggressive treatments, individuals with [kidney disease](#) often experience proteinuria, or excessive loss of protein in the urine, which increases kidney damage. A key factor in the development of proteinuria is endothelin, which by constricting blood vessels and raising blood pressure, causes the kidney's filtering function to deteriorate.

Researchers suspect that blocking the endothelin peptide could be a promising new treatment strategy for patients who develop proteinuria. Endothelin antagonists such as oral avosentan are already available and are prescribed for patients with cardiovascular conditions.

Johannes Mann, MD (Schwabing General Hospital and KfH Kidney Centre, in Munchen, Germany) and his colleagues examined the effects of avosentan on proteinuria and [kidney function](#) in patients with [type 2 diabetes](#) and kidney disease through a multicenter, multinational, double-blind, controlled trial. The Avosentan ASCEND study enrolled 1392 patients already being treated for kidney disease and randomized them to receive avosentan 25 mg, avosentan 50 mg, or placebo.

While avosentan at either dose lowered patients' urinary protein

excretion by 40%-50% (compared with less than 10% in patients taking placebo), individuals taking the drug experienced a high incidence of serious, sometimes life-threatening side effects. These included complications of fluid overload such as pulmonary edema, as well as congestive [heart failure](#). In addition, there were more deaths in the groups taking avosentan (21 and 17) than in the group taking placebo (12).

Dr. Mann noted that the findings from the ASCEND trial highlight the risks and potential benefits of endothelin antagonists in kidney disease patients with proteinuria and will help investigators design future studies to test the drugs' potential. Specifically, lower doses of avosentan may generate more positive results.

More information: The article, entitled "Avosentan for Overt Diabetic Nephropathy," will appear online at jasn.asnjournals.org/ on February 18, 2010, [doi 10.1681/ASN.2009060593](https://doi.org/10.1681/ASN.2009060593) .

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